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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/940,860 | 08/29/2001 | Richard E. Rothman | 001107.00185 | 5063 |

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| EXAMINER | |
|---|---|
| CHUNDURU, SURYAPRABHA | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/940,860 | ROTHMAN ET AL. | |
| | Examiner | Art Unit | |
| | Suryaprabha Chunduru | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,4-23,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23 and 34* is/are allowed.

6)☒ Claim(s) *2, 4-22, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## *DETAILED ACTION*

1. The response filed on June 13, 2006 is entered and acknowledged.

### *Status*

2. Claims 1, 3, and 24-32 are cancelled. New claims 33-34 are added. Claims 2, 4-23, 33-34 are pending and are considered for examination in this office action. This action is made Non-Final.

### *New Grounds of rejections*

3. Claim 33 is objected because claim 33 is dependent on cancelled claim 1.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The meets and bounds of the claim 33 is unclear because the claim is dependent on cancelled claim thus it is not clear what limitations the claim is referring to. Amendment to recite proper dependency would obviate the rejection.

### *Claim Rejections - 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 2, 4, 8, 20-22, 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinman (USPN. 5,516,292) in view of Stratagene Catalog (Stratagene Catalog, page 301-303, 1995).

Steinman teaches a method for performing polymerase chain reaction of claim 2, 4, 20-22, comprising digesting reagents for polymerase chain reaction with a restriction endonuclease (see col. 3, line 1-40, col. 10, line 22-33), wherein the reagents comprise Amplitaq kit reagents (GENEAMP$^{TM}$ PCR Kit reagents) which include Taq DNA polymerase, deoxynucleotide triphosphates (dNTPs) reaction buffer, and a pair of primers (see col. 11, line 37-44,col. 8, 29-36, col. 4, line 38-43, indicating the kit components). Inactivating said restriction endonuclease but not Taq DNA polymerase to form endonuclease-inactivated digested reagents (see col. 11, line 42-44); mixing a test sample and the endonuclease-inactivated digested reagents to form a mixture and subjecting the mixture to conditions such that nay templates present in the test sample hybridized to the primers are amplified (see col. 11, line 45-57, col. 12, line 1-16, indicates that the method follows the methods disclosed in col. 8, line 48-56 for PCR conditions for amplification of the target sample).

detecting amplification product, wherein the detected amplification indicates the presence of template, which hybridizes to both primers in the test sample (see col. 8, line 54-56).

With regard to claim 2, Steinman teaches that also teach restriction endonucleases will not digest primers and the restriction endonuclease is located in the interprimer region, which indicates the primers are have no restriction sites (see col. 9, line 49-54, col. 3, line 33-40, col. 4, line 46-50, indicating restriction sites in the interprimer region, see Fig 2(b) for inter primer region).

With regard to claim 4, 8, 20, Steinman teaches heat inactivation of restriction endonuclease but not Taq DNA polymerase (see col. 11, line 42-44, col. 4, line 1-3). However Steinman did not specifically teach use of Alu I.

Stratagene catalog discloses Alu I (AG/CT) cleaves the double strand sequences and is a type-II restriction endonuclease (page 301).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplification of a target nucleic acid as taught by Steiman et al. with the use of specific restriction endonuclease such as Alu I as taught by Statagene Catalog to achieve expected advantage of developing a sensitive and enhanced method for amplification of target DNA. An ordinary skill in the art would have had a reasonable expectation of success that digestion of PCR reaction mixture with Alu I before PCR amplification would result in an enhanced sensitive detection assay because Stratagene Catalog discloses Alu I has similar activities as restriction endonucleases as taught by Steiman et al. and therefore these restriction enzymes are considered as equivalents. The ordinary artisan would have been motivated to use several such restriction enzymes and such restriction enzymes are

considered functionally equivalent to the claimed restriction enzyme in the absence of secondary considerations.

B. Claims 5-7, 9-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinman (USPN. 5,516,292) in view of Stratagene Catalog (Stratagene Catalog, page 301-303, 306-308, 1995) as applied to claims 2, 4, 8, 20-22, 33 above, and further in view of Hoshina et al. (USPN. (USPN. 5,571,674).

Steinman in view of Stratagene teach a method for performing polymerase chain reaction as discussed above in section 5A.

However, neither Steinman nor Statagene specifically teach the test sample comprising blood, a patient sample, urine, cerebral fluid, primers selected from eubacterial species specific DNA regions, identification of bacterial species by restriction digestion of amplification products.

Hoshina et al. of performing polymerase chain reaction (PCR) comprising

Mixing test sample and the PCR reagents, which include a primer pair to form a mixture (see col. 7, line 21-29, col. 17, line 66-67, col. 18, line 22-25) and subjecting the mixture to conditions such that any templates present in the test sample which hybridizes to said primer pair are amplified and detecting amplification product (see col. 7, line 29-37, col. 18, line 22-28).

With regard to claim 5, 11, Hoshina et al. teach that said sample is a treated blood sample and said treatment comprises extracting DNA therefrom (see col. 18, line 35-40, col. 7, line 21-29);

With regard to claim 6, Hoshina et al. teach that said blood sample from patients suspected of systemic bacteremia (see col. 20, line 22-53);

With regard to claim 7, Hoshima et al. teach primer sequence having (considered as open language as "comprising" ) the sequence as claimed in SEQ ID 1 (see sequence alignment).

With regard to claims 9-10, Hoshina et al. teach that said detection step employs gel electrophoresis and the amplification product is labeled with ethidium bromide and visualized under ultraviolet light (see col. 7, line 34-37);

With regard to claims 12-13, Hoshina et al. teach that said sample is obtained from urine and cerebrospinal fluid (See 18, line 35-43);

With regard to claims 14-15, Hoshina et al. teach that the development of primers hybridize to at eubacterial species' DNA in regions which are highly conserved and comprises 16S RNA genes (see col. 15, line 59-67, col. 16, line 1-6, col. 18, line 25-28, Figs.12-16);

With regard to claims 16-17, 21-22, Hoshina et al. also teach that the method further comprises identifying the bacterial species by sequencing the amplification product or by using restriction endonuclease digestion or restriction mapping that indicates use of one or more restriction endonucleases (see col. 7, line 34-52);

With regard to claim 18-19, Hoshina et al. teach that said method further comprises identifying a bacterial species by amplification of amplified product or amplification of templates in a test sample using primers selected from a single eubacterial species 16S RNA (see col. 19, line 54-67, col. 20, line 1-3, col. 21, line 23-43);

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplification of a target nucleic acid as taught by Steinman in view of Statagene with the inclusion of the target biological samples to

detect bacterial species as taught by Hoshina et al. to achieve expected advantage of developing a sensitive and enhanced method for detecting bacterial infections in biological samples. An ordinary skill in the art would have reasonable expectation of success that the inclusion of said target biological samples as taught by Hoshina et al. would result in an improved and sensitive method for detecting bacteremia in different biological samples such modification of the method is considered obvious the cited prior art. Further, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to use the sequences comprising conserved eubacterial 16S RNA region as taught by Hoshina et al to generate primer pairs to amplify and detect target bacterial nucleotide sequence because Hoshina et al. taught generating such primer pairs using 16S RNA region to amplify species-specific target nucleic acids (see col. 4, Fig. 7). The ordinary artisan would have been motivated to generate a number of primer pairs for detection of target 16S RNA region, such primers and primer pairs are considered functionally equivalent to the claimed primer pairs in the absence of secondary considerations.

***Response to arguments***:

5. With regard to the rejection made in the previous office action under 35 USC 103(a) as being unpatentable over Steinman et al. in view of DeFilippes, Applicants' arguments are fully considered and the rejection is withdrawn in view of the persuasive arguments and new grounds of rejections.

6. With regard to the rejections made in the previous office action under 35 USC 103(a) as being unpatentable over Steinman et al. in view of DeFilippes, further in view of Hoshina et al.,

Applicants' arguments are fully considered and the rejection are withdrawn in view of the persuasive arguments and new grounds of rejections.

***Conclusion***

Claims 23, 34 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru
SURYAPRABHA CHUNDURU
PATENT EXAMINER
9/15/06.